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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,882	11/16/2000	C. Alexander Turner JR.	LEX-0091-USA	5490

24231 7590 06/13/2002

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	10

DATE MAILED: 06/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,882	TURNER ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Claims 1-6 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1 and 2 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the nucleic acids described and the amino acid sequences encoded by them represent splice variants encoded by a single genetic locus, and that the sequences share a common utility as well as substantial structural features, and that a search of SEQ ID NO: 1 and the amino acid sequence it encodes, SEQ ID NO: 2, the Examiner will have effectively searched all of the nucleic acid sequences of the present invention, since SEQ ID NOS: 3, 5, 7 and 9 are all contained within SEQ ID NO: 1, and does not represent an undue burden. This is found persuasive, so all claims will be examined

Claims 1-6 are currently under examination.

Specification

3. The title is objected to because of the word "novel". To obtain a patent, an invention should be novel and the word is therefore redundant.

Claim Objections

4.1 Claim 1 is objected to because of the following informalities: the claim recites "the NHP sequence described in SEQ ID NO: 1", and a sequence is not actually described but is shown or set forth. It is suggested that "described" be replaced with "shown in" as in claims 3-6.

4.2 Claim 1 is also objected to because the name of the protein corresponding to "NHP" should be spelled out in the independent claims where the initials are recited.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1-6 are directed to a nucleic acid comprising the nucleic acid sequence of SEQ ID NO: 1 or nucleic acids encoding the protein of SEQ ID NO: 2, and the splice variants having the amino acid sequences of SEQ ID NOS: 4, 6, 8 and 10, identified as NHPs (novel human proteins). The instant specification discloses that the full length NHP of SEQ ID NO: 2 is a 689 amino acid protein, and that the protein of SEQ ID NO: 2 shares structural similarity with animal *Notch* ligands, and particularly SEL-1 proteins, which are negative regulators of Notch family receptors. The specification asserts that the NHP protein is a member of the *Notch* ligand family due to this amino acid homology Sel-1. Biunno et al., Human Genetics, Vol. 106, pages 227-235, 2000, discloses the human Sel-1 protein, and the attached alignment with SEQ ID NO: 2 shows that there are regions of homology over most of the length of the protein, from amino acids 96-688 of SEQ ID NO: 2, and the entire percent similarity between these two proteins is 46%. However, the NHP nucleic acid molecules or encoded proteins do not have any specific and substantial utility, or a well established utility, as determined according to the current Utility

Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

The instant application describe the uses and methods of the invention, and state that the nucleic acids and proteins can be used in methods such as screening assays to identify receptors, binding proteins, agonists or antagonists which may potentially be drugs, making transgenic animals to also use in screening assays, use of the protein to raise antibodies, use of the nucleic acids to identify mutant alleles, identify polymorphisms, determining the structure of a given locus/allele, expressing the nucleic acid in order to make the protein, or as probes to screen for libraries and isolate clones, or asses gene expression patterns, for example.

However, none of these uses are considered to be specific or substantial utilities for either the nucleic acid molecules or the protein encoded by them. Methods such as identification of receptors, agonists or antagonists, screening for homologous genes, use to identify polymorphisms or alleles, use to recombinantly produce protein or use to generate antibodies are considered general methods applicable to any nucleic acid and/or protein, and are not considered specific or substantial.

The instant application also teaches that the nucleic acids, antisense nucleic acids, protein and associated antibodies, agonists, antagonists can be used either diagnostically to identify mutations, disorders or diseases, and used diagnostically or therapeutically to identify and treat diseases or disorders such as Alzheimer's Disease, diabetes, stroke, vascular dementia, and conditions requiring modulation of fat and cholesterol metabolism such as coronary artery disease.

However, the assertion that the nucleic acids/and or proteins of the instant invention can be used in the diagnosis or treatment of diseases or disorders is also not a specific and substantial utility, and is based on the assumption that the protein is a ligand in the *Notch* ligand family, which as a family are involved in myriad biological pathways and activities. Biunno et al. teach that Sel-1 is ubiquitously expressed in human fetal tissues, but it exhibits high mRNA levels only in adult pancreas and in islets of Langerhans (see page 2), while the instant specification teaches that NHP is expressed in human testis cells. Biunno et al. teach that SEL1 resides on human chromosome 14q24.3-q31, a region linked to an insulin-dependent diabetes mellitus locus, IDDM 11, and on page 2, state that several correlations between mutations in Notch-like genes and pathways to human diseases have been described, and three human disorders including a neoplasia, a late onset neurological disease (CADASIL) and a developmental disorder (the Alagille syndrome) are associated with mutations in, the *Notch1*, *Notch3* and *Jagged1* genes, respectively, highlighting the broad spectrum of Notch activity in humans. On page 7, Biunno et al. state:

> We are studying various aspects of SEL1, both at the structural and functional level, in order to reach a hypothesis regarding the exact role of this protein in cell-cell interaction. At the same time, we are performing association studies in type I diabetic clinical material, such as case control or families, to link polymorphisms and haplotypes of polymorphisms to the SEL1L chromosomal region in order to verify if the gene is responsible for diabetes mellitus type I.

Though sequence homologies may provide information as to the family a protein may belong to, they still do not necessarily predict a function. The SEL1 protein, as evidenced by Biunno et al., does not have a specific known function, and is being investigated further to determine what its function and activities are. The skilled artisan would not be able to predict the

activities or function of the NHP protein based on 46% similarity to the SEL1 protein, because the SEL1 protein also has no known activity, which ***may*** have an association with diabetes mellitus type I.

There is no nexus between any of the diseases or disorders and the molecules of the instant invention. Given no disease state or any other function or activity known for the proteins, the proteins are not considered to have utility. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance, and the use of a protein to discover its receptor or properties does not constitute a specific, substantial utility. All of the biological activities of a protein need not be known to obtain a patent, but there must be some specific and substantial activity or function known. It is possible that after further characterization, this protein might be found to have a patentable utility, in which case the polynucleotides encoding the protein would have a specific utility, or the polynucleotides might be found to be associated with a specific disease. This further characterization, however, is part of the act of invention, and until it has been undertaken the Applicants' claimed invention is

incomplete. Because there is no specific and substantial utility asserted, credibility cannot be assessed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.1 Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the NHP nucleic acid or polypeptide, enablement would not be found commensurate in scope with the claims. If one of skill in the art does not know how to use the nucleic acids or proteins the skilled artisan would clearly not know how to a nucleic acid molecule that comprises 24 contiguous bases of the nucleic acid sequence of SEQ ID NO: 1.

6.2 Claim 2 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO:2, encoded by the nucleic acid molecule shown in SEQ ID NO: 1. However, claim 1 encompasses an isolated nucleic acid molecule comprising at least 24 contiguous bases of the nucleic acid sequence of SEQ ID NO: 1, which encompasses polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that

of SEQ ID NO: 2 and the splice variants, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 2 and splice variants with no disclosed activity, but the claim

encompasses nucleic acids encoding polypeptides that may only have eight amino acids in common with the polypeptide of SEQ ID NO: 2. The specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7.1 Claim 1 is vague and indefinite because it is not clear what "nucleotide sequence **first disclosed** in the NHP sequence" means.

7.2 Claim 1 is also indefinite because it encompasses a nucleic acid molecule which hybridizes under "**stringent**" conditions. Though the specification 4-7 describes various hybridization and wash conditions, they are exemplary. The term **stringent** is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is suggested that the hybridization part of the claim be deleted because hybridization is not a necessary limitation if the key property is what is encoded.

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER